1. The Claims Are Not Anticipated

Claims 19, 21, 25, 29, 30, 35, 38, 40-42, 44, 46, and 47 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gilbert et. al (1993, Transplantation 56: 974-7; "Gilbert") or Adjei (U.S.Patent No. 5,635,161;"Adjei"). Claims 21, 27, 30,32, 38, 40-41, 43-44, and 46-47 are rejected under 35 U.S.C. § 102(b) as being anticipated by Knight et al. (U.S. Patent No. 5,049,388:"Knight") or Waldrep et al.(U.S. Patent No. 5, 958,378;"Waldrep") These rejections are in error and should be withdrawn for the reasons set forth below.

Anticipation requires that all the elements and limitations of the claims be found within a single prior art references. There must be no difference between the claimed invention and the reference disclosures, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 927 F.2d 1565, 18 U.S.P.Q.2d 1001, 18 U.S.P.Q.2d 1896 (Fed. Cir. 1991).

Applicant asserts that the Waldrep, Gilbert and Knight references only disclose compositions comprising liposomal encapsulated cyclosporine. In contrast, the pending claims encompass aerosolized compositions comprising non-encapsulated cyclosporine and the use of such compositions for prevention of graft rejection, pulmonary inflammation and/or inhibition of the immune response associated with T-cell mediated immune disorders using such compositions. Since each of the references fail to disclose the limitation of the claim that requires that the cyclosporine be non-encapsulated, the references simply cannot anticipate the claimed invention. In addition, the Adjei reference only discloses pharmaceutical compositions for aerosol delivery comprising a medicament, a non-fluorocarbon propellant and a vegetable oil.

Therefore, given the differences between the cited references and the present invention, the rejection under 35 U.S.C. § 102(b) should be withdrawn.

2. THE REJECTIONS UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN

Claims 20-48 are rejected under 35 U.S.C. § 103 as being unpatentable over Adjei and Waldrep et al. (U.S. Patent 5,956,378; "Waldrep"), in view of Gilbert, Knight et al. (U.S. Patent 5,049,388) and Applicant's admission on the record.

A finding of obviousness under §103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the difference between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere,* 383 U.S.1, (1996). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. In *re: O'Farrell,* 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Circ. 1988). In addition, "one way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of unexpected results", *In re Soni*, 54 F. 3d 746, 34 U.S.P.Q. 2d 1684 (Fed. Cir. 1995).

In the present instance, the relevant inquiry is whether any of the cited references suggest compositions of non-encapsulated aerosolized cyclosporine and their use for prevention of graft rejection, pulmonary inflammation and/or inhibition of the immune response associated with T-cell mediated immune disorders.

A review of the Waldrep, Gilbert and Knight references reveals that each of the references only disclose compositions comprising liposomal encapsulated cyclosporine. Applicants assert that one of ordinary skill in the art would recognize that encapsulation of cyclosporine into liposomes would materially alter the characterisitcs of the claimed compositions and methods. For example, liposomal formulations containing cyclosporine would have altered pharmacokinetic properties, such as biodistribution, clearance rates, and toxicity as compared to non-encapsulated formulations of cyclosporine. Thus, the mere disclosure of liposomal formulations of cyclosporine would fail to suggest the claimed methods and compositions of the invention, *i.e.*, non-encapsulated formulations of cyclosporine, nor provide any expectation that the claimed methods utilizing such compositions could successfully be practiced.

In addition, although Adjei discloses compositions of non-encapsulated cyclosporine, Adjei fails to disclose or suggest that such non-encapsulated compositions could be successfully used to prevent graft rejection, pulmonary inflammation and/or inhibition of the immune response associated with T-cell mediated immune disorders using such compositions.

In summary, Adjei and Waldrep, in combination with Gilbert and Knight, fail to suggest the compositions of the claimed invention or provide a reasonable expectation of success in the use of such compositions for prevention of graft rejection, pulmonary inflammation and/or inhibition of the immune response associated with T-cell mediated immune disorders. Applicants respectfully request, therefore, that the rejections under 35 U.S.C. §103 be withdrawn.

CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicant believes that the invention described and defined by the claims is patentable. Withdrawal of all rejections and consideration of the new claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

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